Food & Cancer Prevention

Diet can stop cancer before it starts

Prof. Denis E. Corpet

National Veterinary School of Toulouse

UMR ENVT-INRA Xénobiotiques: Aliments & Cancer

Lesson : http://Corpet.net/Denis

Cancer**s** Kill
One Person out of Three

- 100 new colon cancer cases /day in France

  Half of them will survive, half will die **But**

Prevention is possible:

- Lung: 9 out of 10 (at least 90 to 95 %)
- Colon : 3 out of 4 (60 to 80 %)
- Breast : 1 out of 2 (35 to 50 %)

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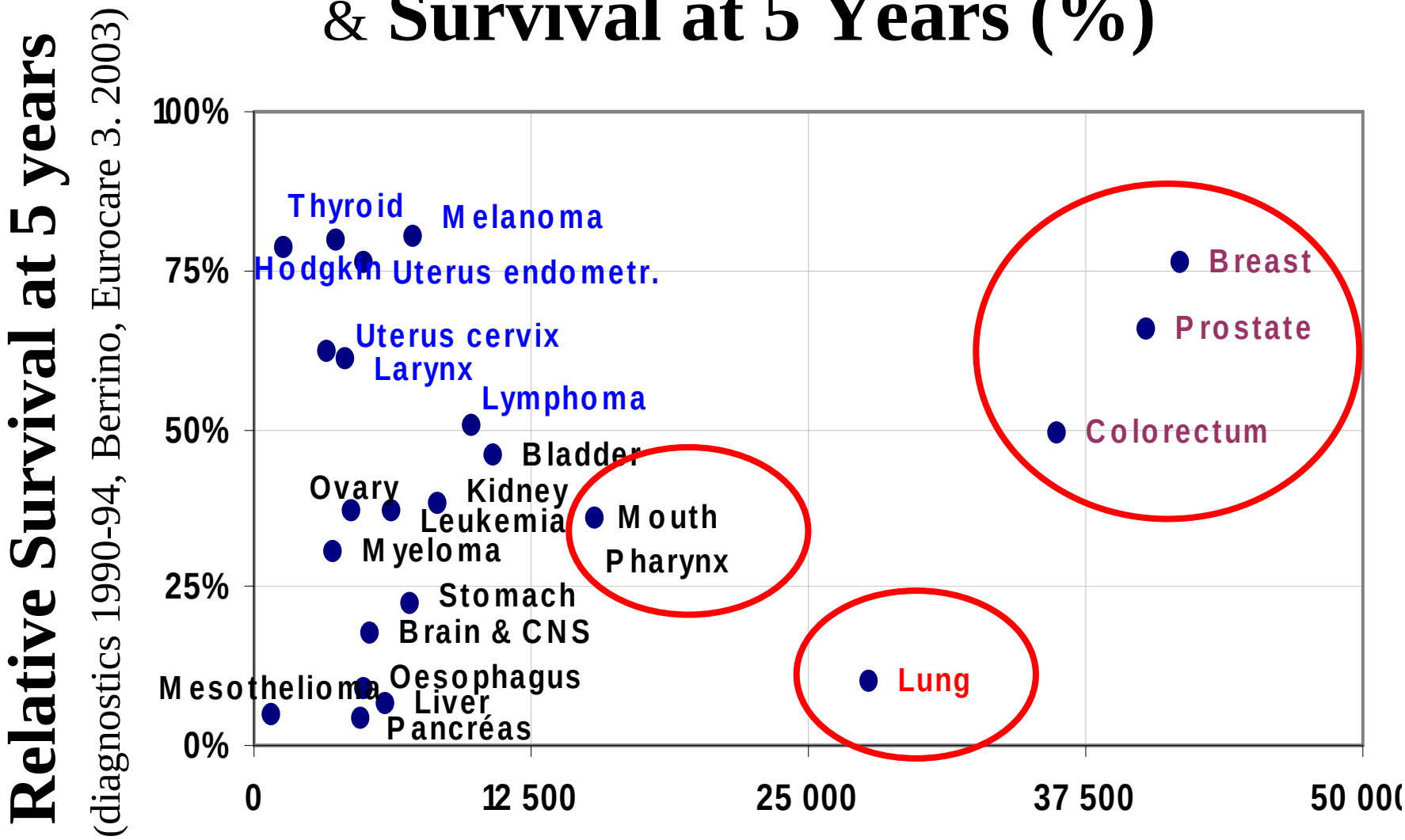
Number of Cancer Cases in France

& Survival at 5 Years (%)



Catherine HILL
IGR, 2005

(Remontet et al. 2002)

Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective

Full Report Online (pdf)

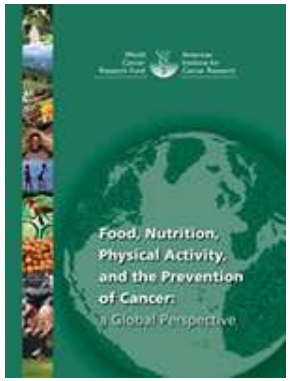
http://www.dietandcancerreport.org

World Cancer Research Fund

American Institute for Cancer Research

WCRF/**AICR** 2007 Report

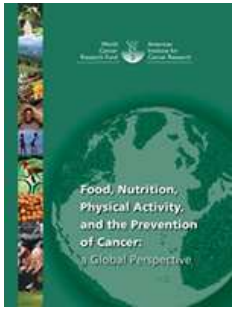
Food & Prevention Cancer



- 1- Lean : Be lean (within normal BMI range)
- 2- Active : Be physically active (in everyday life)
- 3- Low Fat-Sugar: Limit energy-dense foods, no sugar drink
- 4- High Vegs-Fruits: Eat mostly foods of plant origin
- 5- Beef: little, Proces.meat: no Avoid processed meat,
  Limit red meat intake (indiv.< 500 g/wk, group < 300 g/wk)
- 6- Low alcohol: Limit alcoholic drinks (man/woman < 2 / 1 gl/d)
- 7- Low salt, no mould: Limit salt, avoid mouldy cereals
- 8- No Supplements: Meet needs through diet alone
- Mothers to breastfeed / Cancer survivors to follow the above 8s

Five year process: 19 methodologists, **PANEL= 21 top-scientists**,
100 Systematic Literature Reviewers /9 centers,
82 Peer Reviewers & External Contributors. 200 persons x 5 years!

World Cancer Research Fund
WCRF 2007 Expert Report



- 1- Lean
- 2- Active
- 3- Low Fat-Sugar
- 4- High Vegs-Fruits
- 5- Beef: low, Proc.meat: no
- 6- Low alcohol
- 7- Low salt, no mould
- 8- No Supplements
- Mother: breastfeed
- Cancer “survivors”
  same recommendations



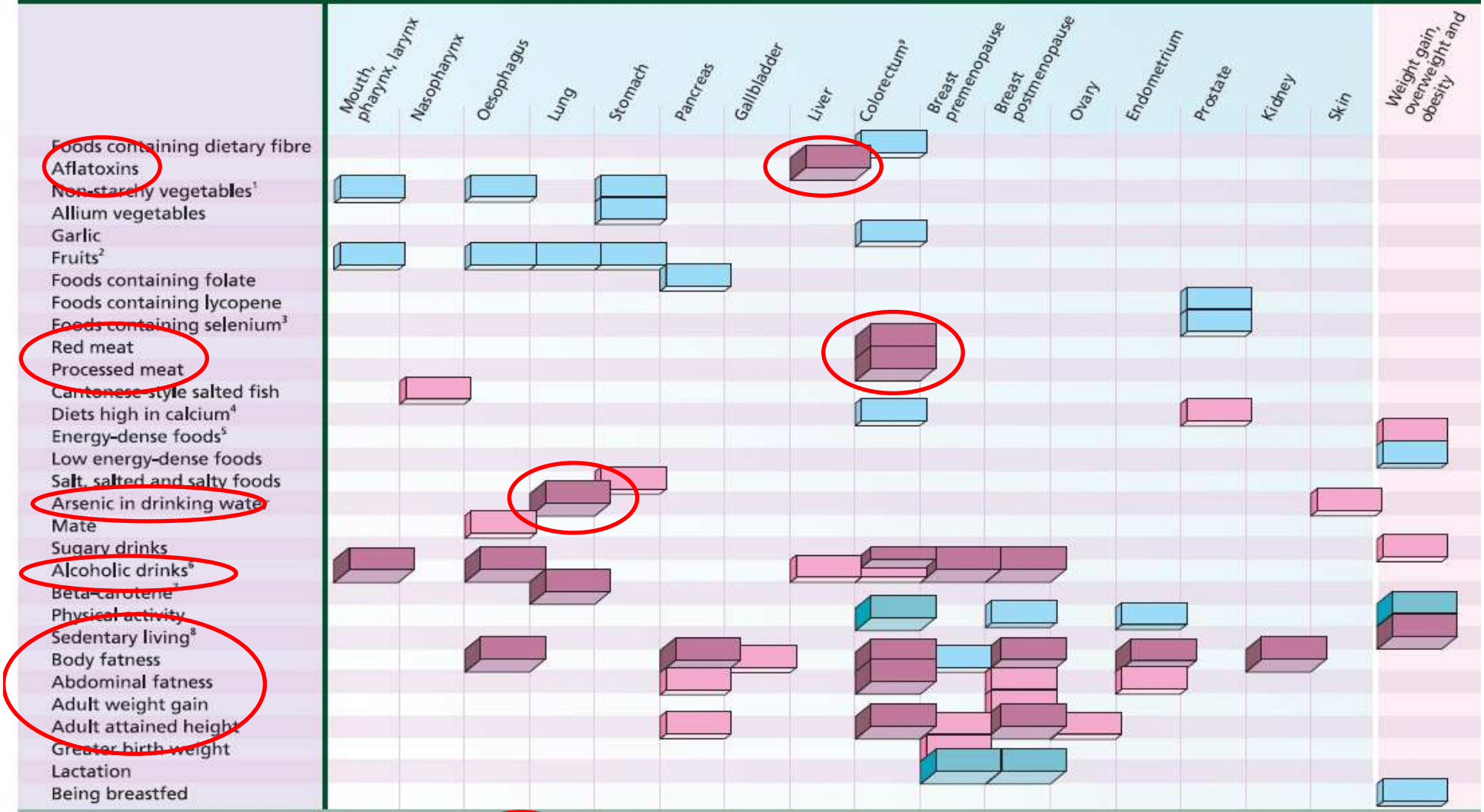







FOOD, NUTRITION, PHYSICAL ACTIVITY, AND THE PREVENTION OF CANCER
OVERVIEW OF THE PANEL'S KEY JUDGEMENTS

Summary of 'convincing' and 'probable' judgements



[1] Includes evidence on foods containing carotenoids for mouth, pharynx, larynx; foods containing beta-carotene for oesophagus; foods containing vitamin C for oesophagus

[2] Includes evidence on foods containing carotenoids for mouth, pharynx, larynx and lung; foods containing beta-carotene for oesophagus; foods containing vitamin C for oesophagus

[4] Evidence is from milk and studies using supplements for colorectum

[5] Includes 'fast foods'

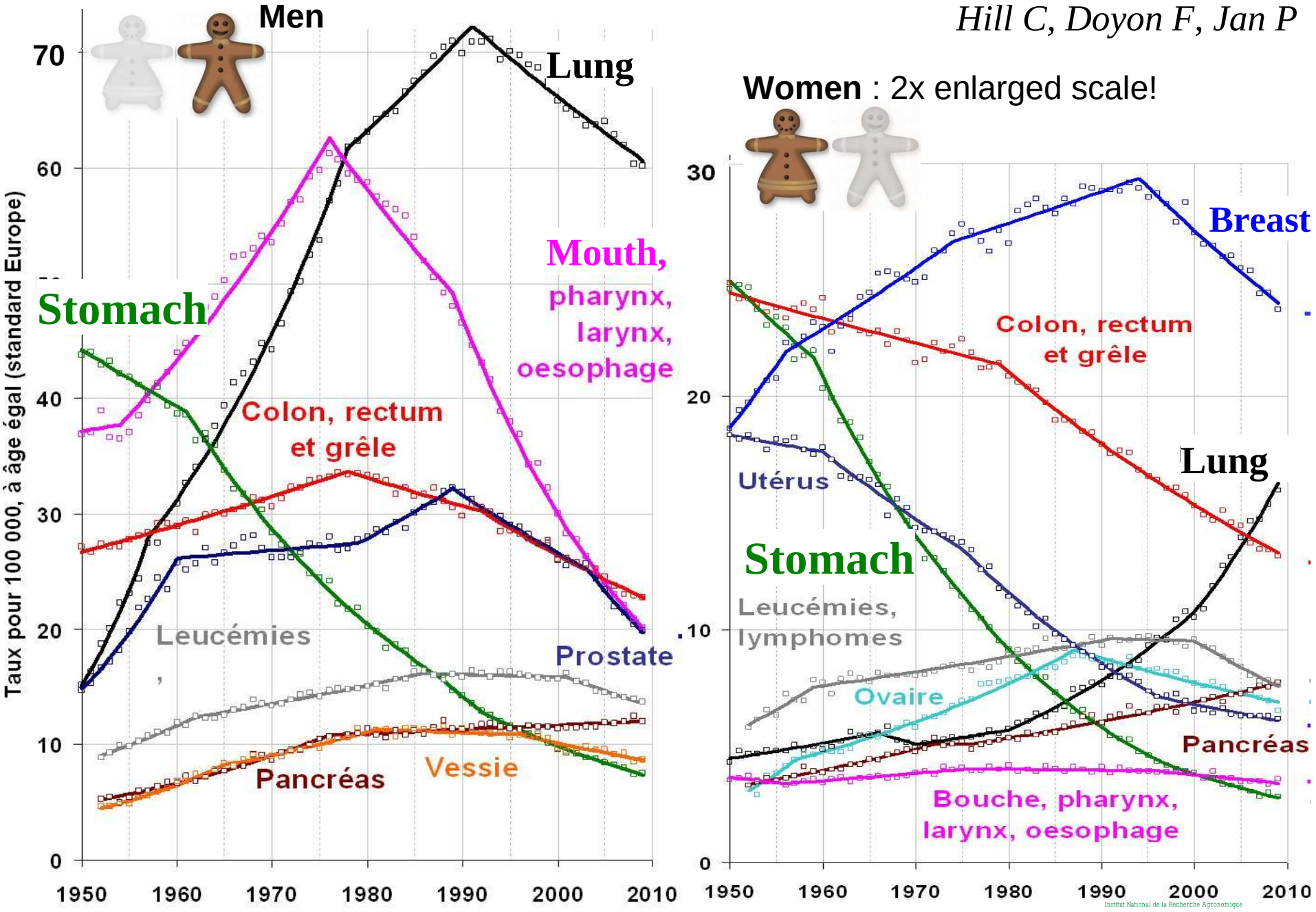
[6] Convincing harm for men and probable harm for women for colorectum

[7] The evidence is derived from studies using supplements for lung

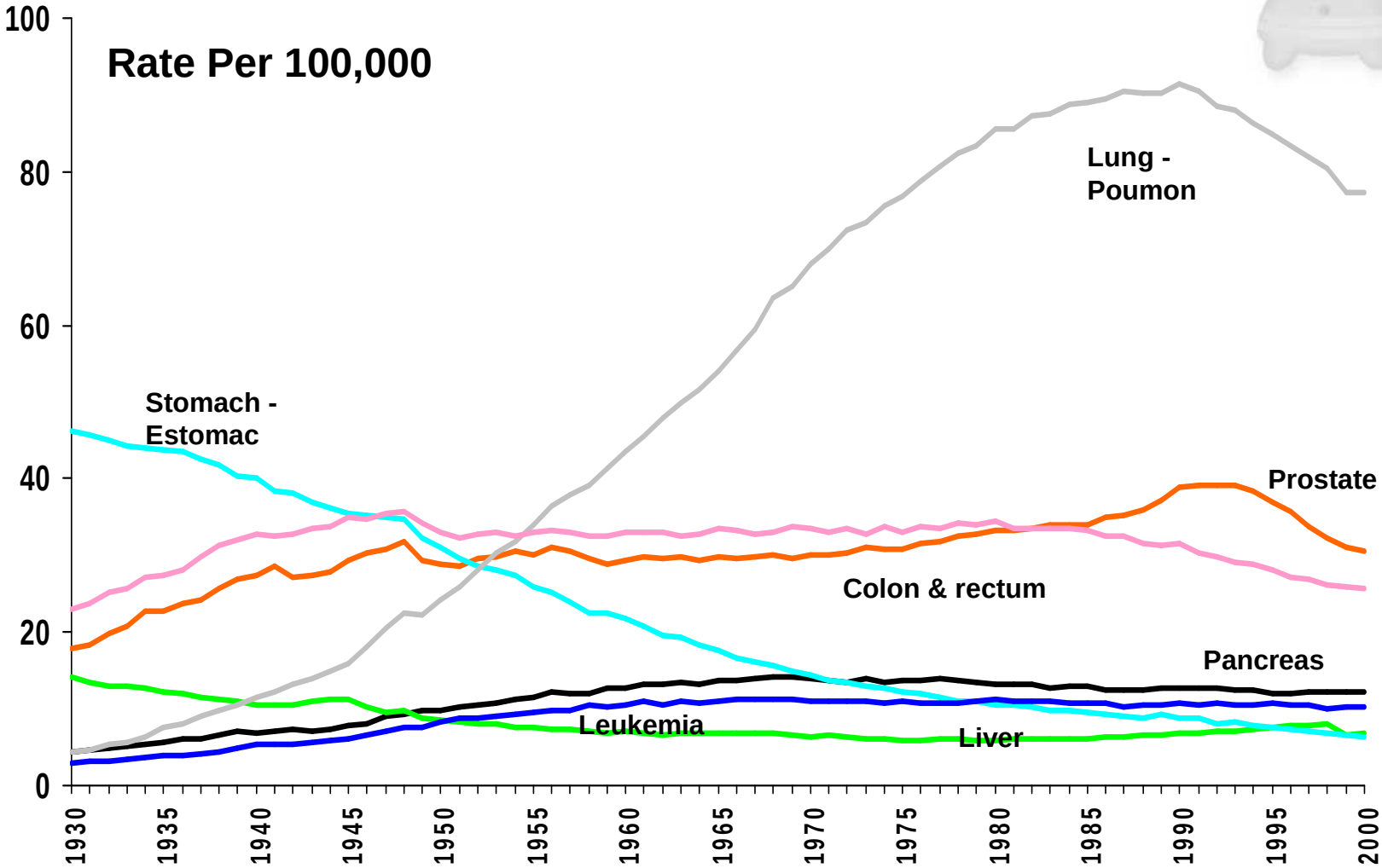
[8] Includes evidence on television viewing

Cancer Mortality - France 1950-2010

Hill C, Doyon F, Jan P

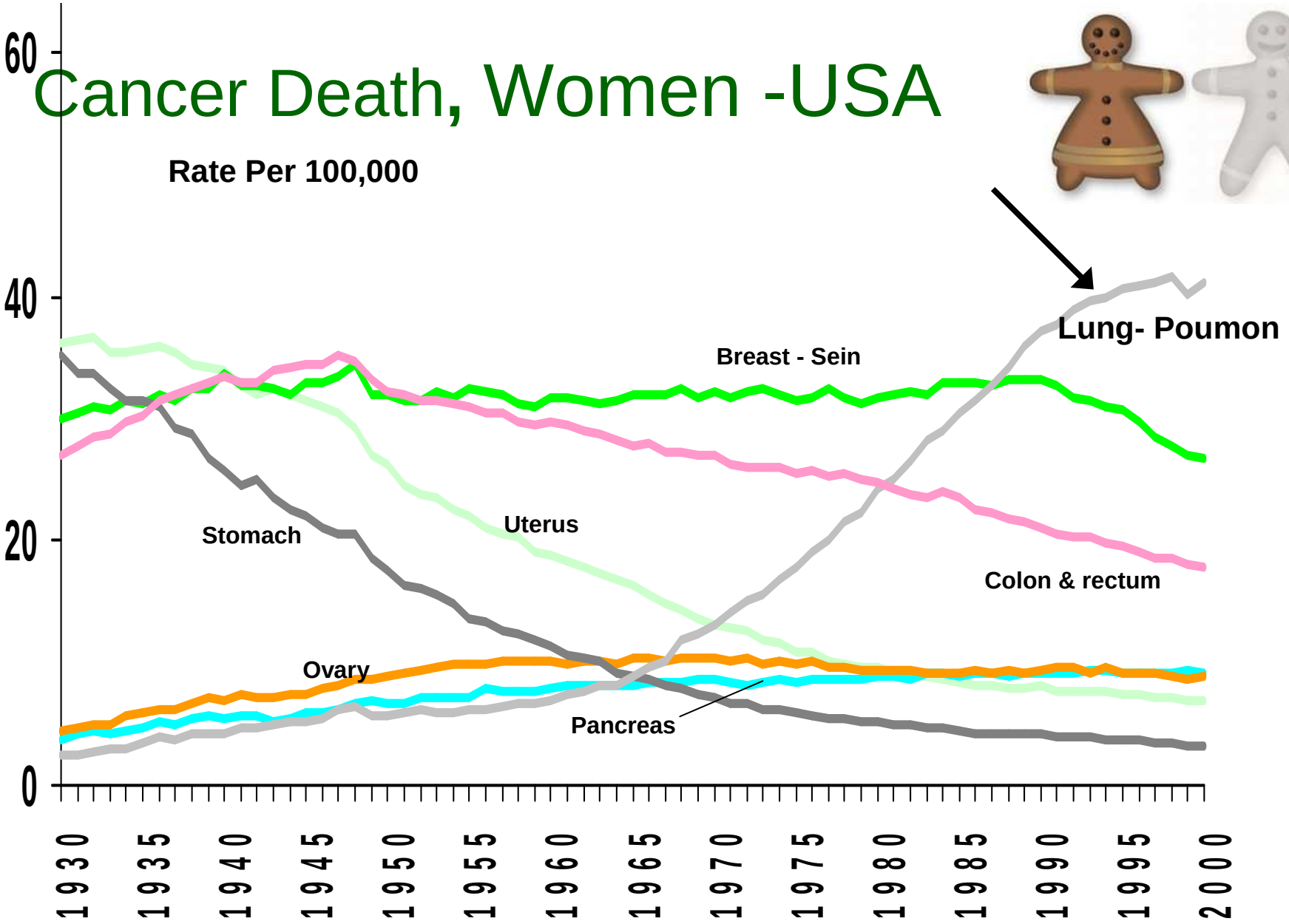


Cancer Death - Men - USA



*Age-adjusted to the 2000 US standard population.
Source: US Mortality Public Use Data Tapes 1960-2000, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2003.

Cancer Death, Women -USA



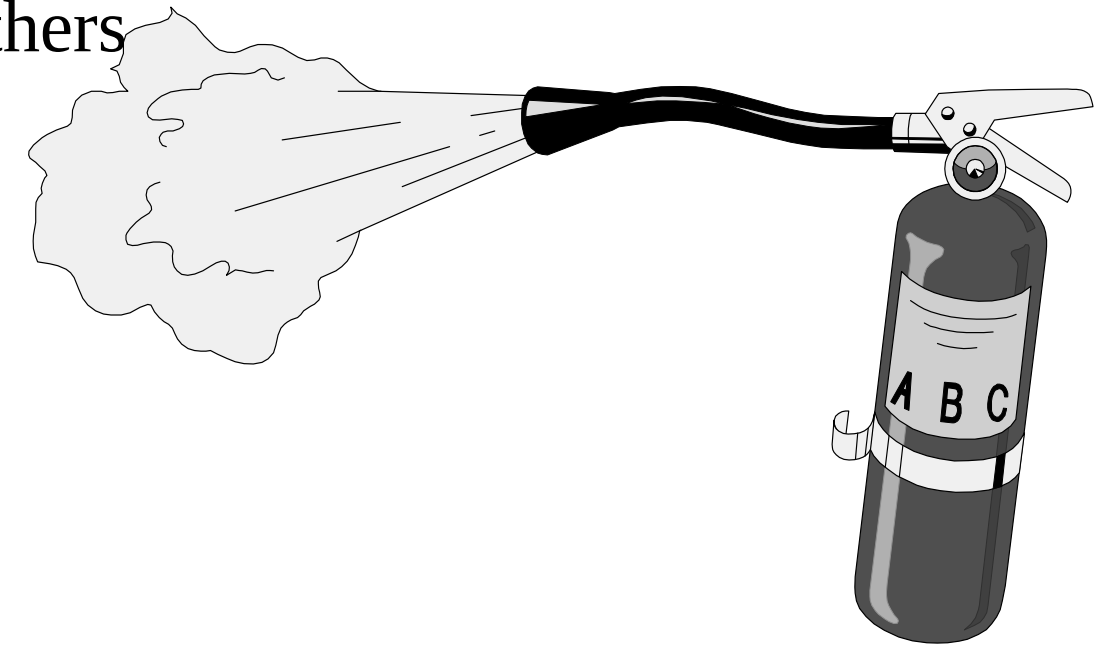
*Age-adjusted to the 2000 US standard population.
Source: US Mortality Public Use Data Tapes 1960-2000, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2003.

Some Cancers Disappear…

- **Stomach** /Refrigerators: more fruits, less salted meat, more hygiene *Helicobacter pylorii*
- **Head & Neck**: less liquor *bouilleurs de cru* (strong alcohol + cigarette)
- **Cervix (neck of the womb)** : hygiene, cervical smear (Pap test) screening, HPV vaccine

Killer n°1: Tobacco Smoke

- Cancers #1 (France & USA) are smokers cancers: Lung, throat, and others …



- We already know:

NO smoking

=

NO Cancer

Cancers:
Not Everywhere the Same

- Affluent Countries, 10 to 20 times more cancers (colon, breast, prostate) than southern countries
- Genetic? seldom
- Migrants catch cancers of welcoming land

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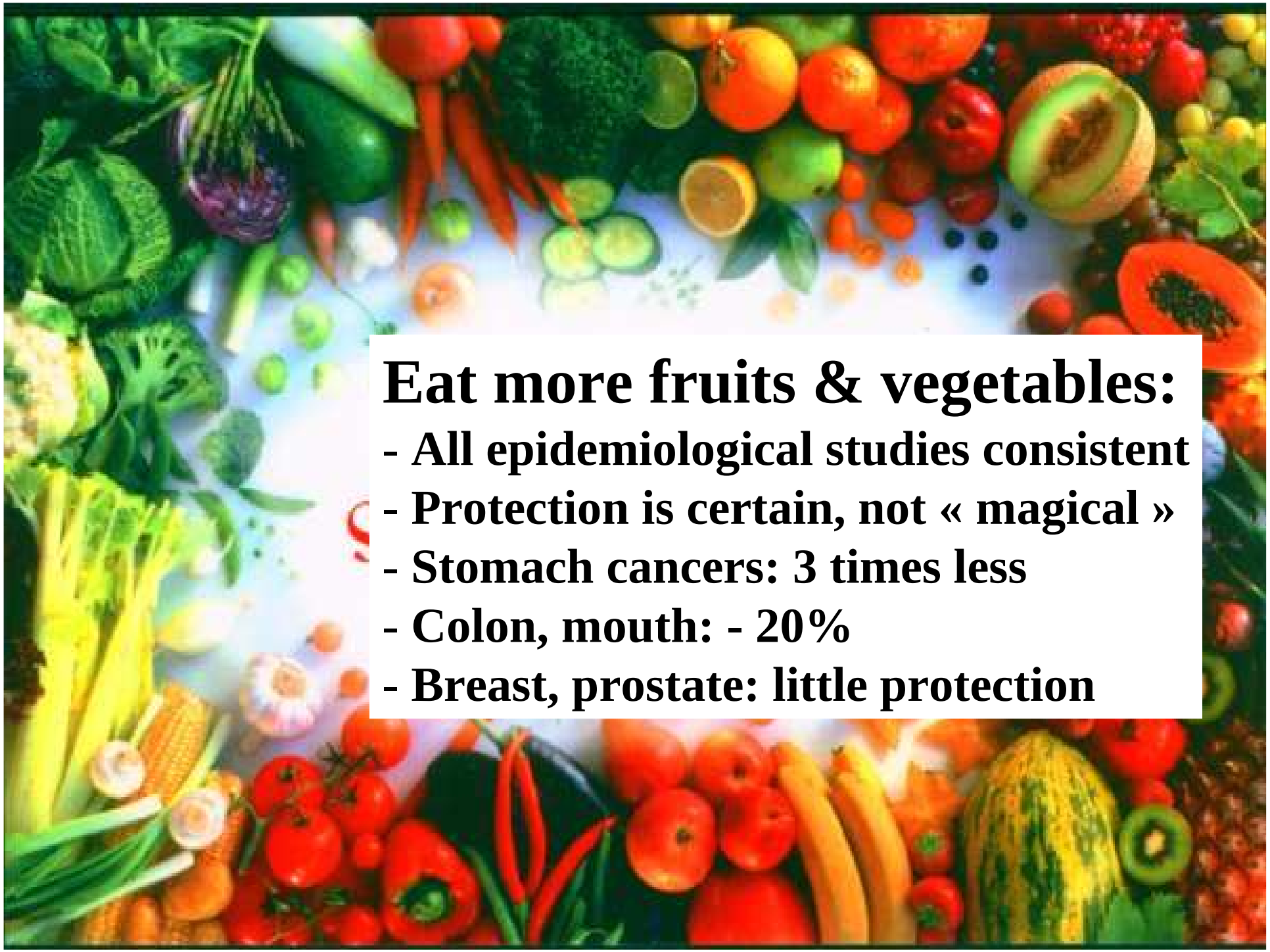
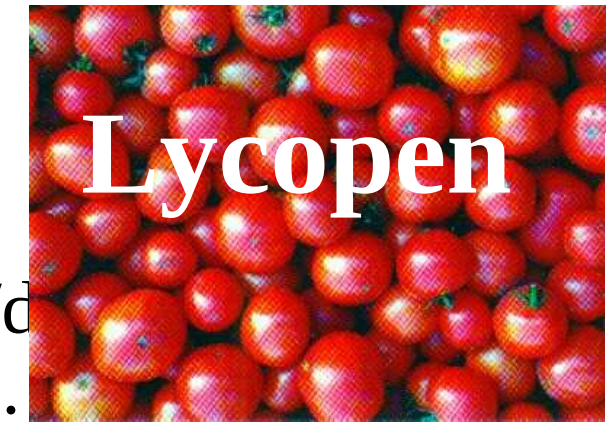
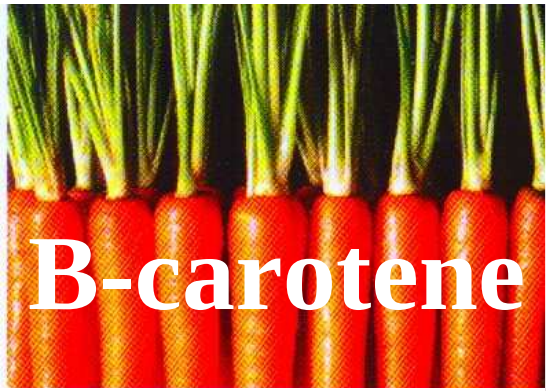

Eat more fruits & vegetables:
- All epidemiological studies consistent
- Protection is certain, not « magical »
- Stomach cancers: 3 times less
- Colon, mouth: - 20%
- Breast, prostate: little protection

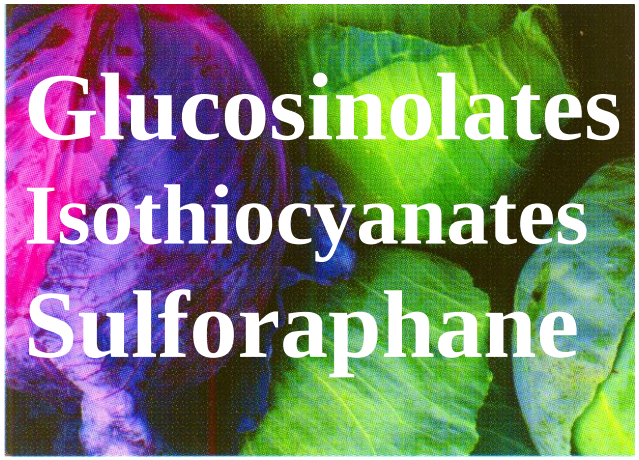
Fruits & Veg.,OK, Which, How Much?

- All, and a lot
- At least five a day, that's 400 to 800 g/d
- All of them, varied:

  Colors & Tastes!







Diapo: Laurence Gamet-Payrastre

Phytochemicals against Cancer? Evidence in Rodents

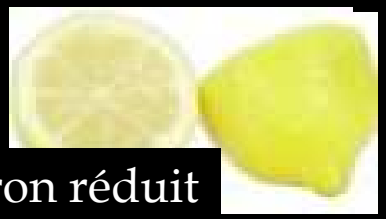
Glucosinolates brocoli diminuent tumeurs mammaires & coliques

Polyphénols cacao bloquent carcinogenèse de la protaste

Anthocyanes des myrtilles diminuent tumeurs du colon

Diallylsulfide de l'ail diminue le nombre de tumeurs colique

EGCG & caféine du thé diminuent tumeurs colon



Pectine citron réduit métastases prostate.
Pectine de pomme diminue cancers poumon & colon

Lycopene des tomates diminue les tumeurs coliques

Curcumine réduit les tumeurs côlon chez rats et souris

Resvératrol du raisin diminue tumeurs colon

What are the Protective Mechanisms?

Diapo:
Laurence
Gamet-
Payrastre

1- Carcinogen trapping

Antioxydant

cancérigène

Polyphénols,
Caroténoïdes
Vitamines C, E

noyau

Sulforaphane
Anthocyanes
DiallylSulfide
Flavonoides
Lycopène

Inactivation
Cancérig

+

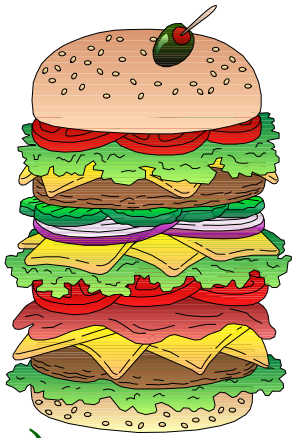
- Glucosinolates
- Sulforaphane
- Flavonoïde
- Sulfide

2- Help to Detoxify

Elimination
dans les urines

3- Block Prolifération (cell growth)
Promote Apoptosis (cell suicide)

- **Physical activity**
  protects (breast, colon)
- **Obesity & Sedentary**
  increase risk
  (post-menopausal breast, colon, uterus endometrium)
- Mecanism: hormones (estradiol, insulin)



Recommendations

- Be lean, do not put weight
- Calories: Eaten = Burned
- Physical activity
  = 5 x 30 min /week (or more)

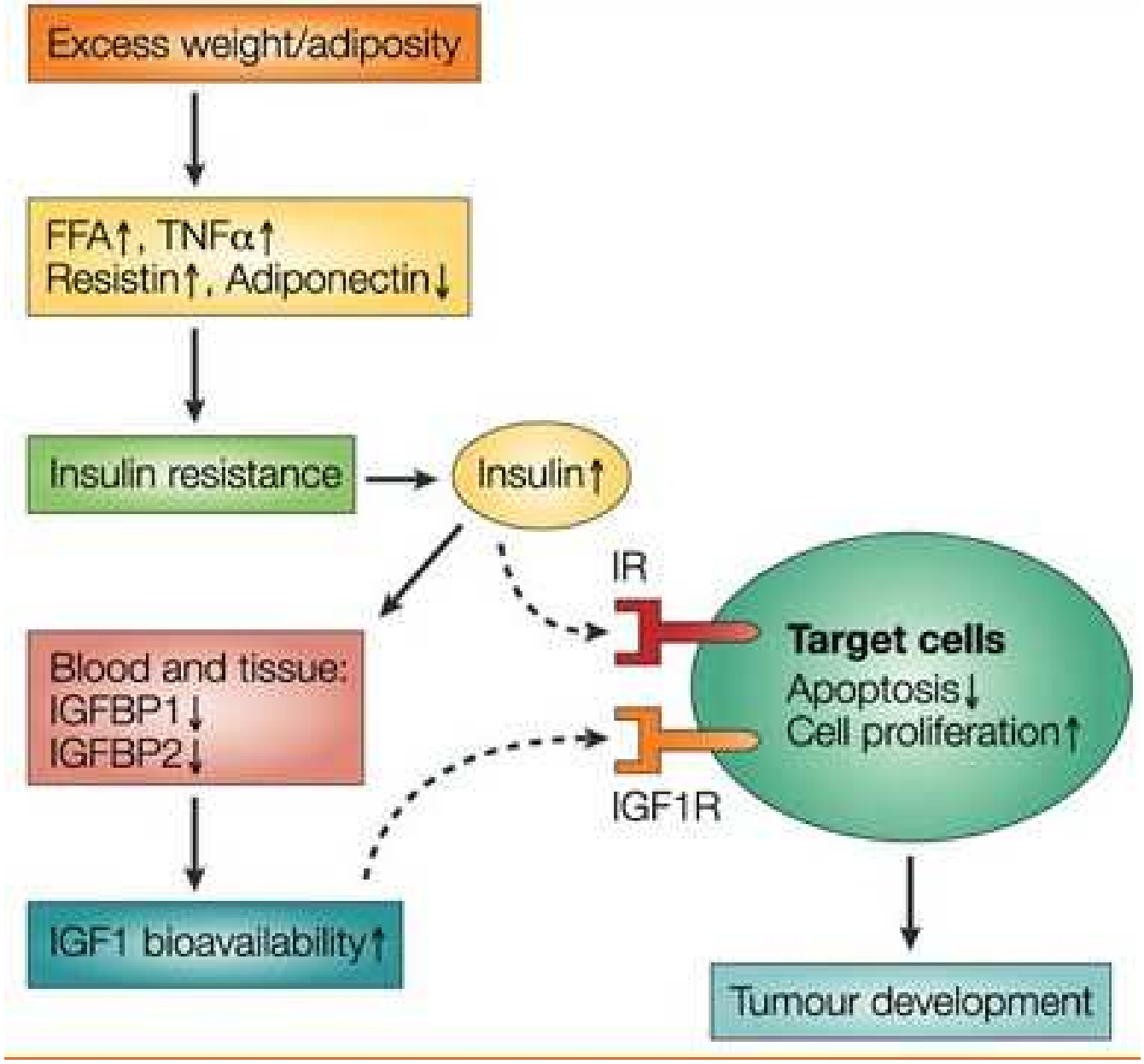
Body fatness & sedentarity convincing causes of colorectal & breast cancer

- Major hypotheses, mechanisms linked to hormones, growth-factors
- Abdominal fat = **insulin resistance** syndrome
- => insulin and IGF1 blood levels are raised.
- **Insulin** & **IGF1** = proliferation of cancer cells *(true at all cancer sites, promotion well demonstrated in colon cancer)*

FFA
Free fatty acids

IGFBP1 & 2
insulin-like
growth factor
binding proteins

Calle & Kaaks,
Nature Reviews
Cancer 2004



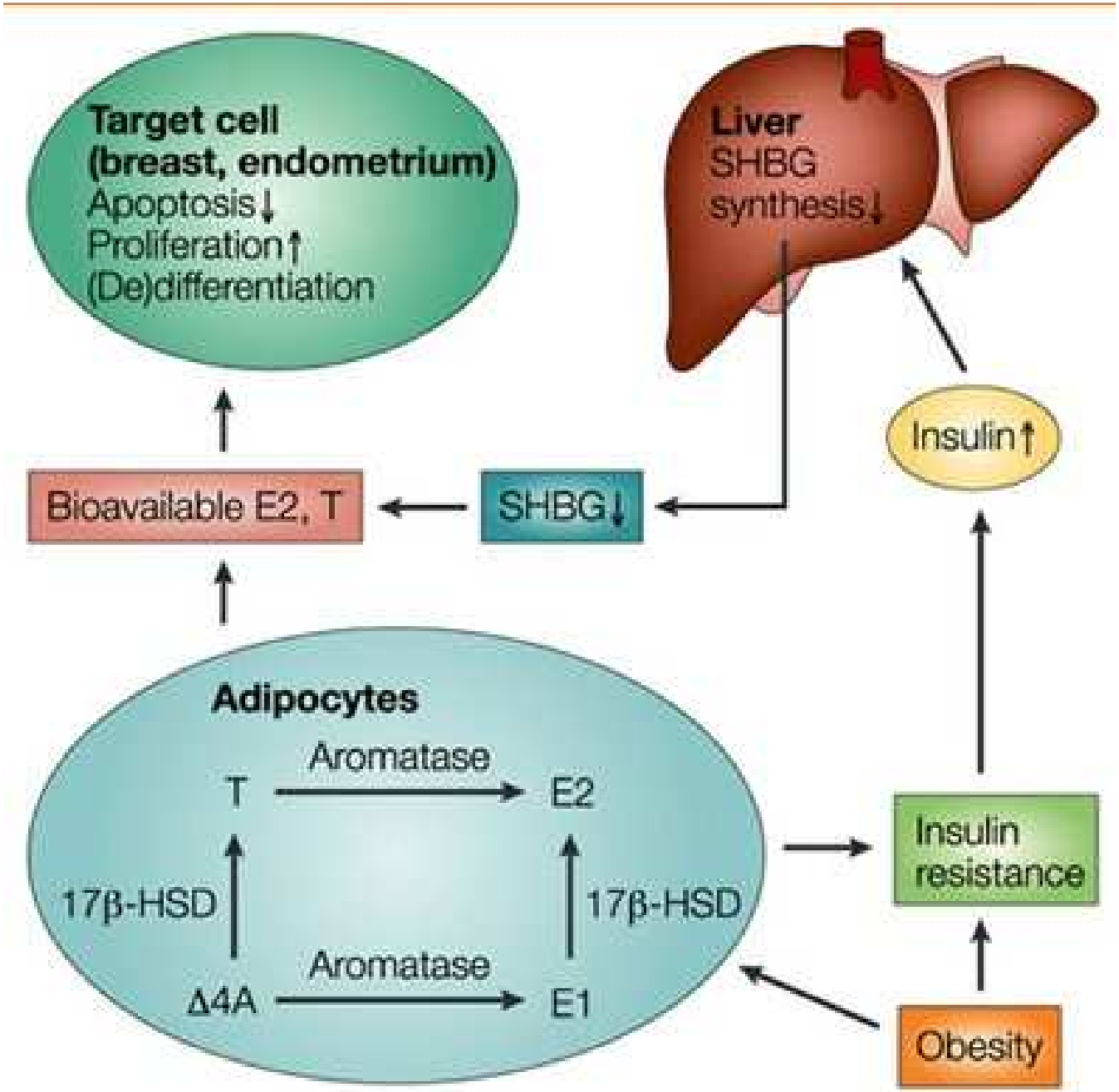
Body fatness convincing cause of cancer
breast **(p.m) &** uterus **endometrium**

- Post-menopause, body fat = major site of steroids aromatisation
- Obese women post-menopause have **increased circulating oestrogens** (oestradiol)
- **Oestradiol** promotes the growth of breast cancer cells (and uterus endometrium cells)

E1, oestrone
=>
E2, oestradiol

deltaA4-androstenedione
=>
T, testosterone

SHBG, sex-hormone-binding globulin



Calle & Kaaks
Nature Reviews
Cancer 2004

Alcohol

There is *sufficient evidence* in humans for the carcinogenicity of alcohol consumption. Alcohol consumption causes cancers of the oral cavity, pharynx, larynx, oesophagus, colorectum, liver and female **breast** (IARC Monographs 2011)

- Mouth, pharynx, larynx, **esophagus** : e.g.,
  1.5 L wine per day =
  20 times more cancer
  than 1 glass a day
- **Breast** :
  3 drinks/d = +50% risk
  10 g/d = + 7-12% risk
- Rectum : beer

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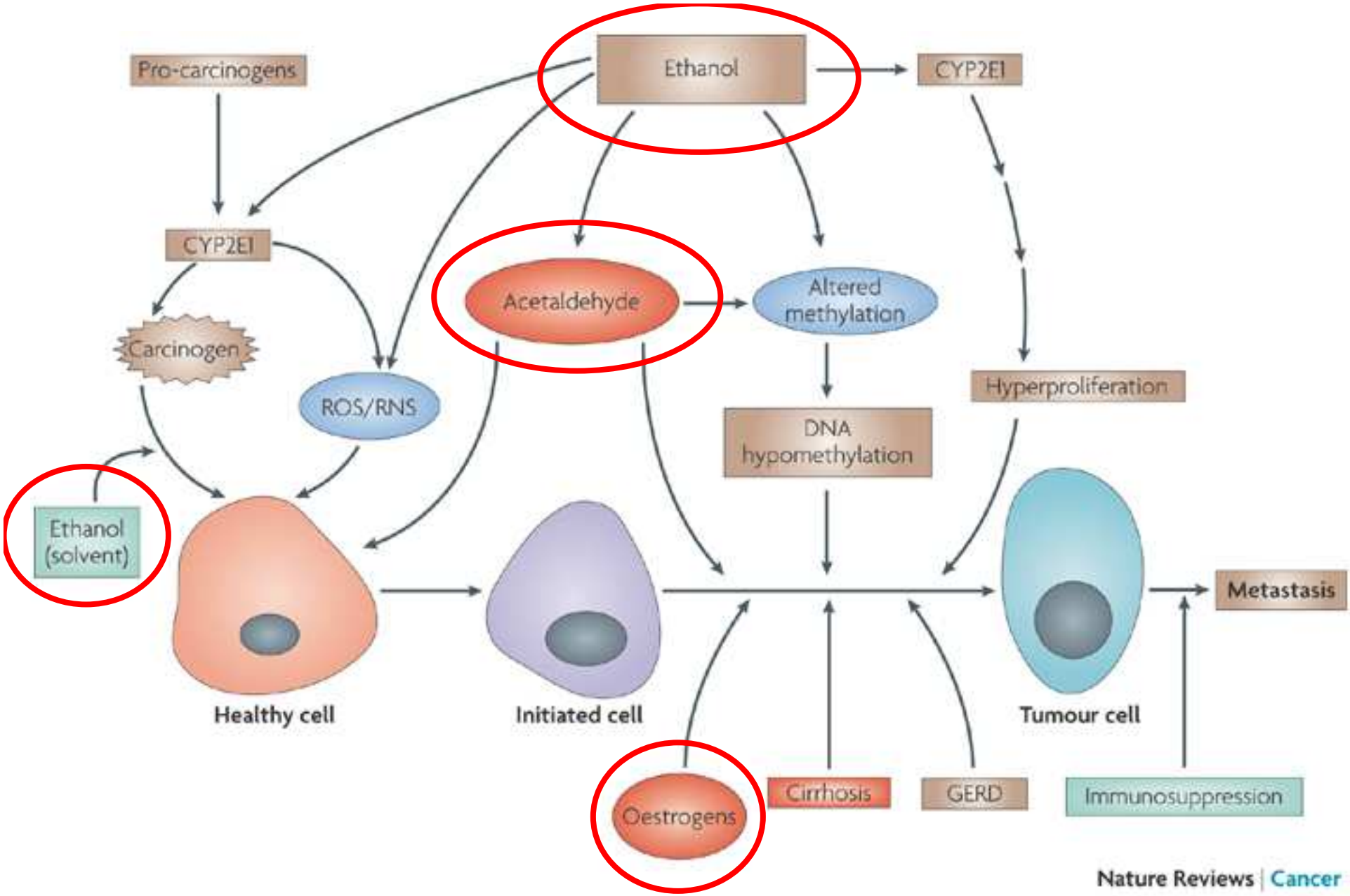
Alcohol, a convicing cause of
head & neck cancers, colorectal cancer, breast cancer

- **Solvent** for tobacco smoke carcinogens
  potent synergy between cigarette smoking & strong spirit drinking

- Oxidized to carcinogenic **acetaldehyde**
  - Alcohol Dehydrogenase (genetic variability)
  - Gut bacteria A.D.ase : acetaldehyde level x1000/blood

- Induces folate deficiency, perturbs **–CH3** metabolism
- Induces lipid peroxides, free-radicals oxygen species
- Interferes with estrogen pathways and reduces immunity



Seitz & Stickel, Nature Reviews Cancer 2007

Fruits & vegs, physical activity, obesity, alcohol, tobacco: **Known effects**

& may be …

- Processed meat favors colorectal cancers
- Red meat too, but smaller effect

RR=1.25
for 125 g/d

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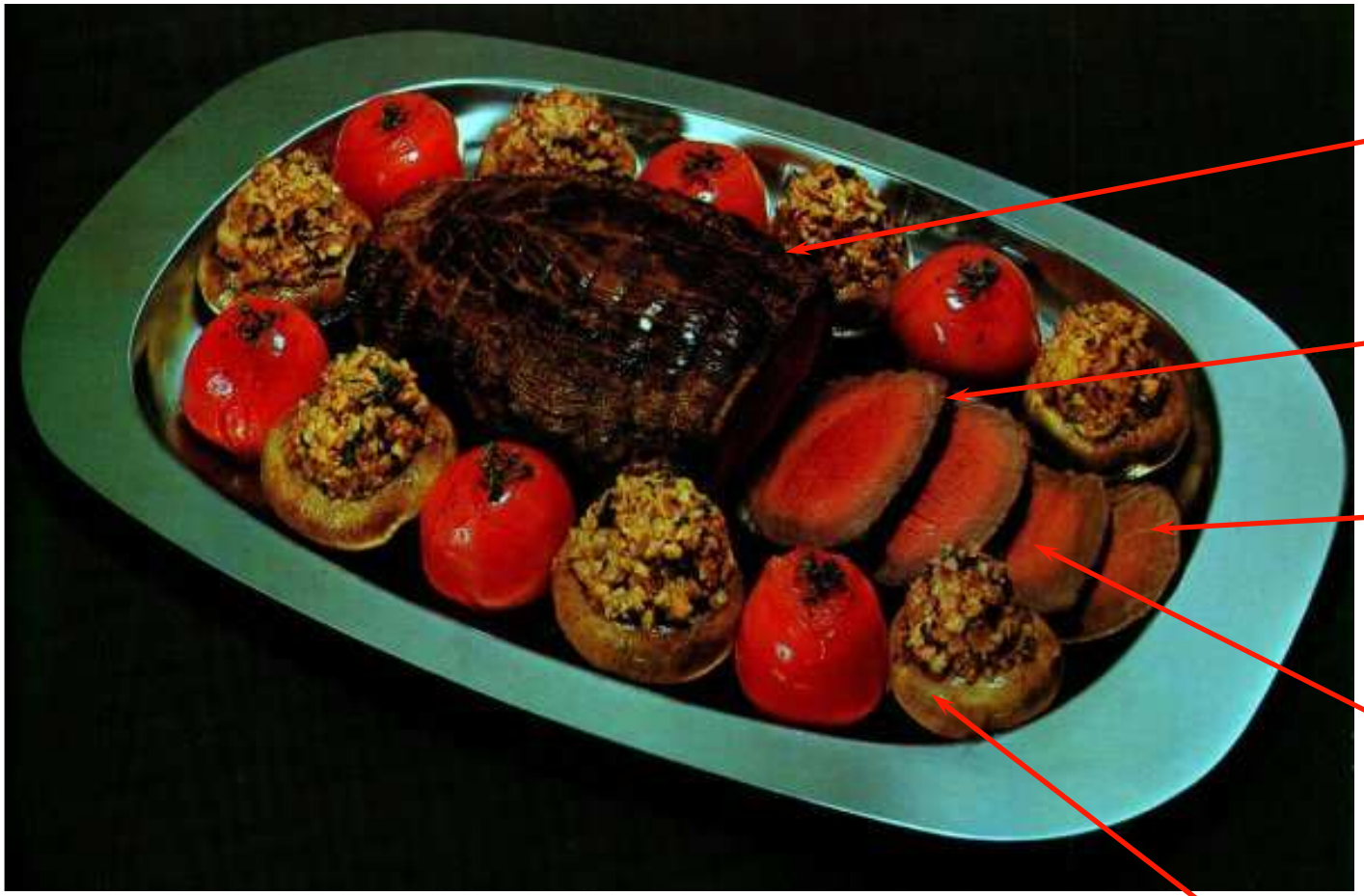
Red Meat, **it is « good » because it is**



Aloyau provencal, «l'art culinaire français», Flamarion 1976

- Grilled
- Fatty
- Protein (Nitrogen)
- Red
- *Veg.deficient*

Processed meat, **more tasty and stable than fresh meat, also contains**

- Salt - NaCl
- Nitrite - $NaNO_2$ & other additives
- Nitrosylated haem & other neoformed compounds

Five Hypotheses / Cancer Red & Processed Meat

- **H1- Red** myoglobin (with haem iron)
  Red/Pink: free **Haem** & nitrosyl haem
- **H2- Nitrogen** & **Nitrite** =
  endogenous amines, ammonia, &
  N-nitrosated compounds (NOC)
- **H3- Cooking** => **Heterocyclic Aromatic Amines** (HAA) & Polycyclic Aromatic Hydrocarbons (PAH)
- **H4- Fat** = too many calories, secondary bile acids
- **H5- Deficient** = not enough protecting agents (calcium, phytochemicals)

H1:

Red Meat

contains

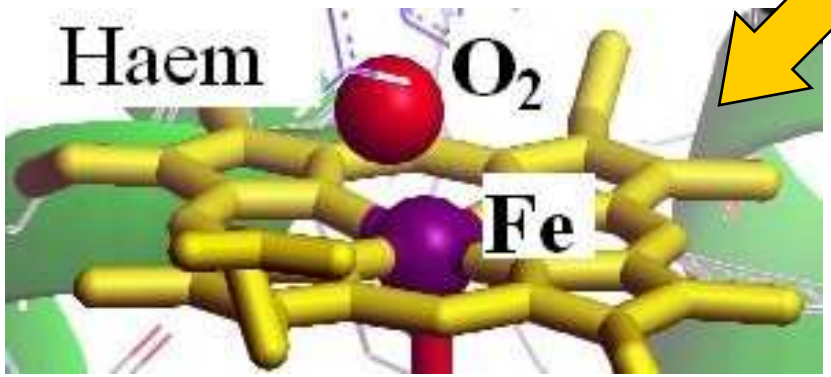
Myoglobin

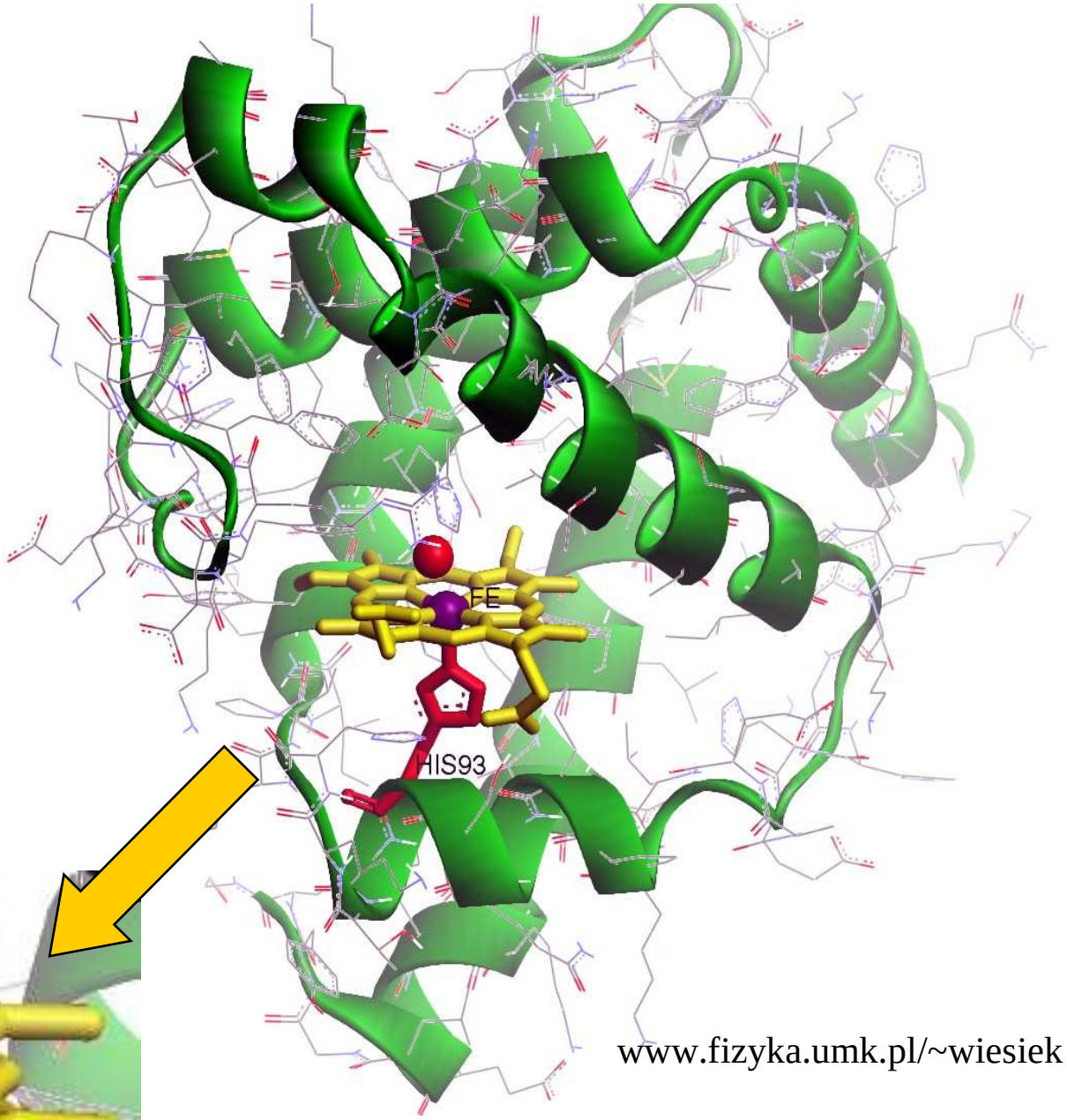
contains

Haem

contains

Iron





www.fizyka.umk.pl/~wiesiek


Denis Corpet


Fabrice Pierre


Raphaelle Santarelli


Océane Martin

Haem iron

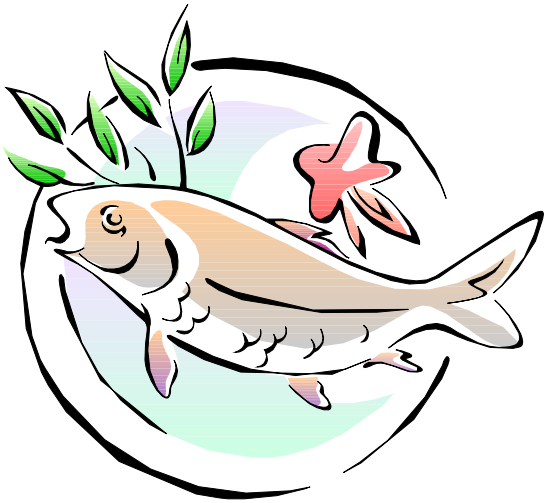
USA: heme, Fr: hème

- **Red meat** contains **myoglobin** (blood haemoglobin)
- **Haemin** induces hyperproliferation & cytotoxicity in rat, inhibited by calcium *(Sesink & van der Meer, 1999)*
- **Haem** induces PUFA oils peroxidation *(Sawa, 1998)*
- Haem loaded foods induces **NOC** formation in volunteers *(Cross & Bingham, 2002)*
- Haemin, Haemoglobin, and Red Meat **promote** precancer lesions in rats *(Pierre & Corpet, 2003-2008)*
- **Iron** (inorganic): No consistent effect on carcinogenesis

Vegetarian? No! (1)

Poultry beneficial ?

- Fish protects ?



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Vegetarian? No (2)

- Red meat is **useful**: It brings iron and vitamin B12 (prevent anemia)

- But do not eat "only" meat, nor too much meat: inverse the meat/vegs ratio

Blessed Fibers?

Satanic Fats?

Fibers would protect

BUT

- Volunteers studies show NO effect of wheat bran supplements!

Fat would promote

MAIS

- Volunteers studies show NO effect of low-fat diet!

Five randomized double-blind placebo-control studies, many years in hundreds of volunteers:
No effect of high-fiber low-fat diets

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Clinical Trials

Randomized, Placebo, Double-Blinded

Several Null Interventions

- Beta-Caroten & Alpha-Tocopherol (Vit.E) :
  More Lung Cancers in B-caroten users for 3 years (+25% & +18%) CARET (USA) & ATBC (Finland)
- Low-fat & high-fiber diets:
  No effect on polyp recurrence 5 years later (Toronto, Brisbane, Alberts, Schatzkin….)
- Vitamin C & E: often tested, no effects!

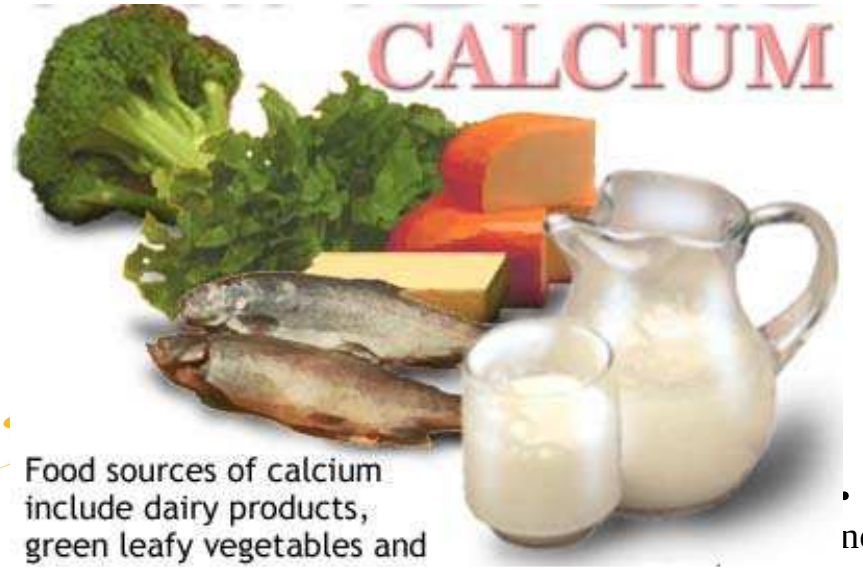
Intervention Studies: Seldom Positives, but …

John Baron, 1999

- **Calcium**
  reduces intestinal polyp recurrence
  (2 g/d carbonate Ca^{++})
- Modest effect (-15%)

Larry Clark, 1996

- **Selenium**
  reduces several cancers incidence (200µg/j selenized yeast)
- Clear effect (-50%) but study not « on purpose »
- But SELECT 2009 contrasts! (purified selenomethionine 35500 men Se/vit.E)



Food sources of calcium include dairy products, green leafy vegetables and

. **Corpet**
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Serge Hercberg's 2004 SUVIMAX Intervention Study

13 000 volunteers

- Daily pill with **nutritional** levels of vitamin C + vit. E + beta-Carotene + Zinc + Selenium
- **One third** less cancers in men
- Male mortality **– 37% !**

SUVIMAX

Carcinogen Potential of Foods

Can we rank carcinogens by potency?

Bruce **Ames** (Ames' test inventor)
& Lois **Gold** (Science 1992, La Recherche 1999)

-Data Base with ALL known rodents' carcinogens
http://potency.berkeley.edu

- Dose-Effect TD_{50}: Tumor Dose 50% =
daily dose yielding a cancer in 50% rats or mice

-Can we extrapolate rodents data to humans?
Compare eaten DOSE (in food),
with carcinogenic dose (in rats)

- HE/RP: **Human Exposure / Rodent Potency**

Carcinogen Potential of Foods

Bruce **Ames** & Lois **Gold** (Science 1992, La Recherche 1999)

HE/RP: Human Exposure/Rodent Potency, TD_{50}: Tumor Dose 50%

Relative Risk HE/RP	**Daily Food intake g/d**	**Carcinogen intake /day**	**TD_{50} mg/kg/d rat-mice**
4,7	Wine (250ml)	Alcohol 30ml	9000
0,1	Mushroom (15g)	Hydrazines 10mg	20000
0,1	Apple (230g)	Cafeic acid 25mg	300
0,07	Mustard (5g)	Isothiocyanate 4,6mg	100
0,03	Spices	Safrole 1.2mg	60
0,03	Peanut butter (32g)	**Aflatoxin** 64ng	**0,003**
0,006	Fried bacon (85g)	diethyl**Nitrosamine** 85ng	**0,02**
0,005	Coffee (4g sec)	Furfural 630µg	200
0,002	AntiOxidant *(additive)*	BHA 700 µg	600
0,001	Tap water (1l)	Chloroforme 83µg	90
0,0003	Carbaryl ***(pesticide)***	Carbaryl 2,6µg	14
0,0001	Fried Salmon (85g)	Me**IQ**x 111ng	**2**
0,00008	DDE/DDT *(pesticide)*	DDE 659ng	12
0,00006	Fried Hamburger (85g)	**PhIP** 176ng	**4**
0,000001	Lindane *(pesticide)*	Lindane 32ng	31

http://potency.berkeley.edu/herp.html

/Google: Ames Gold HERP

Carcinogens

Ranking possible carcinogenic hazards: rodent carcinogens in the American diet (heterocyclic amines in italics)

Possible hazard: HERP (%)	Daily human exposure	Human dose of rodent carcinogen	TD_{50} (mg/kg) Rats	Mice
4.7	Wine (250 ml)	Ethyl alcohol, 30 ml	9110	(–)
0.3	Lettuce, 1/8 head (125 g)	Caffeic acid, 66.3 mg	284	(4970)
0.1	1 Mushroom (15 g)	Mix of hydrazines, etc.	(?)	20,300
0.1	Basil (1 g of dried leaf)	Estragole, 3.8 mg	(?)	52
0.07	Mango, 1 whole (245 g; pitted)			
0.07	Brown mustard (5 g)			
0.06	Diet cola (12 oz; 354 ml)			
0.06	Parsnip, 1/4 (40 g)	8-Methoxypsoralen, 1.28 mg	32	(?)
0.03	Safrole: US avg from spices	Safrole, 1.2 mg	(436)	56.2
0.03	Peanut butter (32 g; 1 sandwich)	Aflatoxin, 64 ng	0.003	(+)
0.03	Comfrey herb tea (1.5 g)	Symphytine, 38 μg	1.91	(?)
0.006	Bacon, pan fried (85 g)	Diethylnitrosamine, 85 ng	0.02	(+)
0.005	Coffee, 1 cup (from 4 g)	Furfural, 630 μg	(679)	197
0.003	1 Mushroom (15 g)	Glutamyl *p*-hydrazino-benzoate, 630 μg	(?)	277
0.003	Bacon, pan fried (85 g)	*N*-nitrosopyrrolidine, 1.45 μg	(1.05)	0.679
0.002	Apple juice (6 oz; 177 ml)	UDMH, 5.89μg (from Alar, 1988)	(–)	3.94
0.002	Bacon, pan fried (85 g)	Dimethylnitrosamine, 255 ng	(0.2)	0.2
0.002	Coffee, 1 cup (from 4 g)	Hydroquinone, 100 μg	82.8	(225)
0.002	Coffee, 1 cup (from 4 g)	Catechol, 400 μg	226	(–)
0.001				
0.001				
0.0005		*p*-Hydrazinobenzoate, 165 μg	(?)	454
0.0003	Carbaryl: daily dietary avg	Carbaryl, 2.6 μg (1990)*	14.1	(–)
0.0002	Toxaphene: daily dietary avg	Toxaphene, 595 ng (1990)*	(–)	5.57
0.0001	*Salmon steak, baked (3 oz; 85 g)*	*PhIP, 306 ng*	4.29[a]	(28.6)[a]
0.00008	*Salmon steak, baked (3 oz; 85 g)*	*MeIQx, 111 ng*	1.99	(24.3)
0.00008	DDE/DDT: daily dietary avg	DDE, 659 ng (1990)*	(–)	12.5
0.00006	*Hamburger, pan fried (3 oz; 85 g)*	*PhIP, 176 ng*	4.29[a]	(28.6)[a]
0.00003	Whole wheat toast, 2 slices (45 g)	Urethane, 540 ng	(41.3)	22.1
0.00003	*Hamburger, pan fried (3 oz; 85 g)*	*MeIQx, 38.1 ng*	1.99	(24.3)
0.00002	Dicofol: daily dietary avg	Dicofol, 544 ng (1990)*	(–)	32.9
0.00002	Cocoa (4 g)			
0.000005	*Hamburger,*			
0.000001	Lindane: dai			
0.0000004	PCNB: daily dietary avg	PCNB (Quintozene), 19.2 ng (1990)*	(?)	71.1
0.0000001	Chlorobenzilate: daily dietary avgan	Chlorobenzilate, 6.4 ng (1989)*	(–)	93.9
<0.00000001	Chlorothalonil: daily dietary avg	Chlorothalonil, <6.4 ng (1990)*	828	(–)
0.000000008	Folpet: daily dietary avg	Folpet, 12.8 ng (1990)*	(?)	2280
0.000000006	Captan: daily dietary avg	Captan, 11.5 ng (1990)*	2690	(2730)

Natural Carcinogens , plants

Processed-food Carcinogens, meat cooking

Contaminant Carcinogens, pesticides

Same carcinogen potency

One glass of **wine**	➢contains 13 g **alcohol**
150 **bread** *baguettes*	➢contains 200 mg **furfural** (weak carcinogen in crust)
7000 grilled beef **steaks**	➢contains 1 mg **PhIP** (potent carcinogen)
25 million **apples** pesticide-treated	➢contains 3 g **Captan** (pesticide in fruit skin)

*Carcinogen Potency Database: B.N. **Ames**, HERP, Berkeley 2003*

Conclusions

- **Yes,** Fruits & vegetables, physical activity, protect against cancers.
- **Yes,** it is better not to gain weight, to eat little (processed) meat, to drink little alcohol, and to do **not smoke at all**
- This **halves cancer risk**: hard to believe but true!
- And everything else that you may read or be talked might be true, but **is not demonstrated yet!**

Conference is online
http://Corpet.net/Denis/

Bon appétit !

ECOLE NATIONALE VETERINAIRE TOULOUSE

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Food & Cancer - 2013

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